MNETHOD AND APPARATUS FOR THE DIAGNOSIS OF GLAUCOMA AND OTHER VISUAL DISORDERS

1   Method and Apparatus for the Early and Rapid

2   Diagnosis of Glaucoma and Other Human and Higher

3   Primate Visual Disorders

4

5   This invention relates to methods and apparatus for

6   assessing eye function. The invention is useful

7   *inter alia* in the diagnosis of glaucoma and other

8   visual disorders, and in the assessment of dyslexia

9   and neurological conditions which affect eye

10   function.

11

12   The common form of glaucoma, as is typical of

13   several other visual disorders, is a progressive

14   disease. Currently the disease can be arrested but

15   not cured. Symptoms include the gradual reduction in

16   the field of view of the affected eye progressing in

17   a characteristic pattern. Due to the nature of the

18   human visual system, victims of the disease do not

19   typically notice this reduction in field of view

20   until the disease has already progressed for several

21   years. Instruments exist which can measure the

22   field of view of a patient but all available

23   instruments suffer from three major problems that

24   limit their utility in making an early diagnosis.

1　　First they are both low in resolution and

2　　inaccurate. This low resolution means that the slow

3　　progression of the disease at typically 1.8% of the

4　　field of view per annum can take several years to be

5　　detectable. (See for example "Relative rates of disc

6　　and field change examined in eyes at high risk"

7　　C Scerra, <u>Ophthalmology Times</u> 15/10/2001)

8

9　　Secondly the existing devices and methods are slow

10　　and complex in clinical use and hence expensive in

11　　practitioner time. This means that even those

12　　practitioners who possess a field of view analysis

13　　device cannot economically use it as a routine

14　　screening device.

15

16　　Thirdly the existing instruments are inherently

17　　expensive and so are not as widely available as is

18　　required for the widespread screening necessary for

19　　early diagnosis.

20

21　　At one time it was thought that measurement of

22　　eyeball pressure would provide a method for early

23　　diagnosis of glaucoma but this has proved unreliable

24　　as the correlation between pressure and glaucoma has

25　　proved not to be as high as was originally thought.

26　　Instruments for the measurement and mapping of the

27　　sensitivity of the human retina known as "visual

28　　field analysers" or "Static Auto-perimeters" have

29　　hitherto required that the subject perform very

30　　unnatural and often uncomfortable eye behaviours

31　　such as long periods of attempted fixation on a

32　　point. Additionally, hitherto such instruments

1　depended on tests requiring a voluntary response

2　from the subject. The subject is asked to

3　concentrate on a fixation point and report on the

4　presence and position of stimuli presented to their

5　peripheral vision. This process is both slow and

6　prone to inaccuracy.　The ability of the subject to

7　accurately fixate is also known to be poor

8　especially over an extended period and so the

9　accuracy of a purely fixation point to stimulus

10　measurement is further compromised.

11

12　This invention substantially reduces or eliminates

13　these problems and introduces an entirely novel

14　method and apparatus that allows the subject under

15　test to behave completely naturally (in the sense

16　that they are not required to suppress natural

17　visual reflexes) which both improves accuracy and

18　lowers the stress on the subject. Furthermore the

19　disclosed method and apparatus greatly reduces the

20　time required to map the visual field, which makes

21　the test far more economic and practical for routine

22　screening than the existing equipment that requires

23　lengthy tests under expensive expert supervision.

24

25　　　　　　　　　　**BACKGROUND TO THE METHOD**

26　While eye to hand co-ordination and reaction is

27　relatively slow and subject to variability and

28　improvement from practice, and eye to voice reaction

29　time is even slower, the reaction time of the eye

30　itself to stimulus is extremely fast in humans and

31　primates. The eye muscles reflexively react to

32　stimuli without the need for conscious action by the

1 subject. Although this reflex can be consciously

2 overridden, the nature of the stimulus and prior

3 fixation can be engineered by methods disclosed in

4 this invention to ensure that the reliability

5 exceeds 97 percent. Furthermore, because the eye

6 reflex is inherently faster than eye-hand or eye-

7 voice reaction times, any variability in the

8 response has a far lower impact on the accuracy of a

9 reaction dependent measurement. This allows the

10 apparatus to exploit the time information in a

11 variety of ways to increase the data obtainable from

12 each individual test point.

13

14 The invention, which is defined in the appended

15 claims, is based on the use of an eye position-

16 measuring device capable of measurement of eye

17 position at intervals of less than 45 ms, of which

18 several types are commercially available, in

19 conjunction with a display unit capable of

20 displaying a multiplicity of visual stimuli and

21 capable of accurate calibration of luminance

22 sufficient to exceed the desired accuracy of the

23 desired test. The device is configured to detect the

24 rapid motion of the eye (known as a saccade) towards

25 a new stimulus and to use this saccade to determine

26 the moment the subject's visual reflex responds to

27 the stimulus. Since the subject need not consciously

28 respond to the stimuli the entire field of view

29 measurement process can be automated. By way of

30 example, a set of stimuli can be presented, each

31 stimulus initially below expected threshold

32 increasing in brightness until the stimulus triggers

1   the reflex saccade of the eye from a fixation
2   stimulus. The time the reflex saccade is detected is
3   used to determine the threshold of the retina for
4   that point. The eye position-measuring device can in
5   a preferred embodiment be used to check that the
6   eye's saccade did in fact occur in the correct
7   direction confirming that the test stimulus and not
8   another distraction caused the saccade. At the
9   moment of the said saccade the stimulus that was the
10   saccade target transforms into the fixation point
11   for the next stimulus. This is an important feature
12   for two reasons.
13
14   First, the accuracy of immediate post saccade
15   fixation has been shown to be consistently many
16   times better than long term fixation on a single
17   point, and secondly the visual process of saccading
18   from one stimulus to another in sequence is the
19   normal visual scanning mode of the human and higher
20   primate eye, hence the experience for the patient
21   feels natural and unforced, especially if the
22   frequency of the induced saccade is designed to be
23   equivalent to the normal scanning saccade frequency
24   of the eye. This normal scanning frequency varies
25   from time to time in a given individual and from
26   individual to individual but the invention also
27   discloses a method that allows the practitioner to
28   quickly determine this value accurately. Setting the
29   saccade frequency perfectly is not generally
30   necessary but will help to make the test more
31   accurate particularly with anxious patients.
32

1   A major advantage of this method of field of view

2   measurement over the prior art is that it eliminates

3   the need for very large samples to be gathered for

4   each stimulus position and repetitive confirmation

5   of the subject's observation of the stimulus and the

6   reliability of their visual fixation. This vastly

7   reduces the time needed for a diagnostician to

8   establish a subject's field of view.

9

10   In preferred forms, the invention exploits a

11   detailed computer model of the human visual system's

12   autonomic reflex timings and uses a response

13   interpolator based on this model to allow more

14   accurate interpretation and extrapolation from data

15   while ensuring that the conditions of the test more

16   closely approximate normal visual tasks. This

17   improves both the comfort of the subject and

18   accuracy of the test results. The invention allows

19   sufficient accuracy to determine progression from

20   one test to another of a fraction of a percent,

21   takes little clinical time to administer and the

22   apparatus itself is economic and easily affordable.

23

24   In addition to the above benefits the nature of the

25   disclosed method and apparatus also has utility in

26   diagnosis of other visual disorders not directly

27   related to visual field but still dependent on the

28   exploitation of the computer reflex model. This

29   allows the invention to be applied to the diagnosis

30   of high function visual disorders such as dyslexia

31   and visual "neglect". Dyslexia is a higher brain

32   function disorder, which can be improved by

1　appropriate training, and "neglect" is a symptom of

2　a particular form of brain damage.

3

4　SUMMARY OF THE INVENTION

5

6　The invention provides a method as defined in claim

7　1, apparatus as defined in claim 24, and also a

8　software package as defined in claim 42.

9

10　Preferred features of the invention and benefits

11　thereof will be apparent from the subordinate claims

12　and from the description.

13
14　DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS OF THE

15　INVENTION

16

17　Embodiments of the invention will be described, by

18　way of example only, with reference to the

19　accompanying drawings, in which:

20

21　Fig. 1 is a schematic illustration of one

22　apparatus embodying the invention; and

23　Figs. 2 and 3 represent images used in one

24　method according to the invention.

25

26　Prior to this invention visual field analysis

27　methods and apparatus have been extremely crude, in

28　general consisting of an array of lights or other

29　display illuminated under a pseudo-random protocol

30　and at varying brightness straddling the expected

31　threshold of the retina and a fixation point to

32　attempt to maintain some minimal knowledge of the

1   eyes position prior to stimulus. Unfortunately the
2   human vision system is particularly poor at
3   maintaining a constant fixation and furthermore even
4   if this is achieved with practice there are side
5   effects to concentration on a fixation point that
6   significantly reduce the accuracy of the
7   measurement. As a consequence most of these machines
8   are, in practice, little better than the intelligent
9   use of a pen waved at the subject by the
10   practitioner. They provide a rough map of defective
11   areas but the positional accuracy of the defect
12   perimeter is grossly compromised by the
13   impossibility of accurate fixation maintenance by
14   the subject and furthermore the nature of a pursuit
15   or fixed fixation task in itself causes large
16   variations in the subjects' apparent peripheral
17   retinal sensitivity. In research applications with
18   volunteer subjects who are practiced in the use of
19   the instrument these instruments do provide useful
20   data but as a routine diagnostic tool they are
21   simply too complex, time consuming and difficult to
22   use for both the practitioner and the patient.
23
24   The following references confirm this assertion:
25
26   "Selective Peripheral Fading:
27   Evidence for Inhibitory Effect of Attention on
28   Visual Sensation"
29   Lianggang Lou
30   Department of Psychology
31   The University of Hong Kong
32

1   Barbington-Smith B, 1961 "An unexpected effect of
2   attention in peripheral vision" *Nature (London)* 189
3   776
4
5   Duncan J, 1980 "The locus of interference in the
6   perception of simultaneous stimuli" *Psychological*
7   *Review* 87 272-300
8
9   The prior art of which the following small sample is
10 typical, ignores the nature of the human visual
11 system as a whole. In the absence of such a model
12 the measured values for a given point in the field
13 of view will be tend to be grossly inaccurate both
14 spatially (topologically) and in amplitude terms.
15 The results are akin to plotting the chart of a
16 shoreline with an elastic plumb line and a faulty
17 sextant.
18
19 As stated above the prior art consists primarily of
20 various methods of presenting varying brightness
21 stimuli to the eye from various angles depending on
22 some form of fixed or moving reference fixation
23 point to deliver geometric accuracy or they include
24 some form of eye tracking system which requires a
25 calibration that is itself subject to the same error
26 of fixation as the untracked test. All of the prior
27 art requires significantly abnormal eye behavior
28 from the subject under test over typically tediously
29 long periods. As the above references show such
30 abnormal fixation behavior inherently destroys both
31 the topological and amplitude accuracy of the data
32 being collected to the point where it is accepted in

1 ophthalmic diagnosis that the repeatability of the

2 measurements can not be better than plus minus 5

3 degrees and plus minus 2.5dB. Given the progress of

4 common glaucoma at 1.8 percent per annum this means

5 in practice that a confirmed diagnosis of glaucoma

6 can take the several years required to establish the

7 nature of progression with such low repeatability

8 instruments.

9

10 EXAMPLES OF THE MOST COMMONLY USED PRIOR ART

11 US4561738: Field tester

12 Humphrey; William E., San Leandro, CA

13 Campbell; Charles, Berkeley, CA

14 US5050983: Visual testing method and apparatus

15 Johnson; Chris A., Davis, CA

16 Shapiro; Lionel R., Davis, CA

17 US5024519: Apparatus and method for visual-field

18 testing

19 Howard; Dwight L., Winters, CA

20 Johnson; Chris A., Davis, CA

21 _____

22 The present inventors theorised that if a test

23 method could be devised that allowed the patient to

24 behave as naturally as possible it would

25 consequently be true that the patient's autonomic

26 responses would more reliably follow normal

27 repeatable curves. The inventors also researched

28 both fixation and stimulus methods that promote

29 relaxed natural reflex saccades. By carefully

30 researching the limit and variability of these

31 normal responses it would be practical to gather

1 information about the eye's sensitivity and visual

2 field from careful timing of the natural saccade

3 responses to stimuli. This could be applied to

4 several visual stimuli ranging from a carefully

5 sequenced repetitive single point stimulus similar

6 to a conventional visual field analysis method to

7 the presentation of specially formatted images or

8 video sequences where the saccade timing variation

9 between a normal and a visually impaired individual

10 could be made readily apparent.

11
12 This theory was subsequently proved to both the

13 inventors' satisfaction and led to the present

14 invention.

15

16 Referring to Fig. 1, one embodiment of apparatus for

17 use in the invention comprises a display screen 10

18 viewed by a subject 12. Any suitable display may be

19 used which is capable of presenting images where the

20 luminance of any point in the image over the desired

21 field of view can be defined at least as accurately

22 as the desired amplitude accuracy of the desired

23 retinal map. Preferably, the display is capable of

24 presenting an animated fixation image consisting of

25 a substantially stationary central region comprising

26 at least 20 percent of the diameter of the fixation

27 image, and a mobile perimeter defined such that the

28 perimeter is less than 3 degrees of the arc of

29 vision of the subject in diameter. By way of

30 example, such a fixation image might consist of an

31 insect such as a ladybird with wiggling legs acting

32 as the mobile perimeter, or in a more abstract form

1   a central disc with an eccentric ring with the

2   perigee rotating about the central disc.

3

4   An eye position sensor 14 detects movement of the

5   subject's eye. The sensor should be capable of

6   measuring eye position at intervals of less than

7   45ms. Several types of sensors meeting these

8   requirements are available commercially.

9

10 The eye motion sensor typically comprises a video

11 camera connected to a computer, in combination with

12 software executed by the computer. The software

13 compares each new frame of the video output from the

14 camera to an average of a previous plurality of

15 frames, typically two to five video frames depending

16 on required sensitivity and speed of response. The

17 frames are compared in terms of each RGB value for

18 each pixel and a threshold difference is set

19 determining the change in RGB value that constitutes

20 a motion fast enough to be a saccade of the pupil.

21 The averaging of the previous group of frames

22 eliminates noise differences and the threshold

23 determines both the magnitude and speed of a motion

24 in the frame. The video cameras are mounted on a

25 headset and may be wirelessly connected to the

26 computer, suitably via a 1.2 or 2.4 GHz wireless

27 video link. Suitable cameras are available from

28 Ajoka, Swan and Sony. Sony cameras can also be run

29 at very high frame rates and so can improve

30 accuracy. The eyes are preferably illuminated with

31 infra red light so that the image is monochrome

32 whether the camera is colour or not.

1

2   A distance sensor 16 monitors the distance between

3   the subject and the display in at least the z-

4   direction (i.e., the direction orthogonal to the

5   left/right and up/down movements of the subject's

6   eye). The distance sensor is preferably one which

7   is non-contact and thus does not restrain head

8   movement, for example ultrasonic ranging, laser

9   ranging, stereo or mono video perspective analysis,

10   suitable forms of which are available commercially.

11   Contact means which do not unduly constrain head

12   movement may also be used but are not preferred.

13

14   Typically, the z-measurement is made by an

15   ultrasonic ranging system coupled to the computer

16   (e.g. via RS232), available from Miford Instruments

17   as one example. However, alternative ranging systems

18   could be used. One option is a second video camera

19   mounted on the test screen top centre and connected

20   to the computer (e.g. via USB), which detects the

21   pupils of the eyes using an infra red source co-

22   axially mounted with the camera lens via a beam

23   splitter, or simply placed as close to the lens as

24   possible. This produces bright spots at the pupils

25   as seen by the camera (the same effect that causes

26   "red eye" in a flash photograph). The camera image

27   can be adjusted via brightness and contrast and

28   suitable infra red pass filters so that only the

29   pupils are seen in the image as two bright dots.

30   Software determines the distance between the two

31   dots. Suitable software is commercially available

32   but is also easy to write from scratch. One supplier

1   of suitable software, called Common Vision Blox, is

2   Image Labs International, Montana USA, who also

3   produce software components suitable for use in the

4   motion detection previously described. In use, the

5   optician enters the Inter-Pupil Distance to the

6   system and the z-distance can then be calculated

7   from knowledge of the apparent separation of the

8   pupils, the focal length of the lens and the size of

9   the image sensor.

10

11 A control means 18 controls the display on the

12 screen 10 and receives and processes data from the

13 sensors 14 and 16, in particular data relating to

14 the timing and direction of saccades following the

15 presentation of stimuli. Comparison means 20

16 compares this data with a library of information

17 held in a database 22, and results are output to a

18 recording or display means 24. The various elements

19 18, 20, 22, 24 may suitably be incorporated within a

20 general purpose computer.

21

22 Unlike the prior art, the present invention uniquely

23 exploits an accurate model of the autonomic visual

24 reflexes and interrelated aspects of visual

25 perception in humans and higher primates to vastly

26 improve the accuracy and repeatability of the

27 measurement. This model is incorporated in the

28 timing versus illumination increments described in

29 the method. Additionally, the natural interaction of

30 the device with the subject eliminates stress and

31 fatigue in the test that further enhances the

32 repeatability. Uniquely, after rapid basic mapping

1   of the visual field the device allows the detailed

2   plotting of any portion of the retina such as the

3   perimeter of a defect to a repeatable accuracy of a

4   fraction of a degree, allowing defect progression

5   rates of 1 degree per annum or less to be detected

6   and characterised by tests separated by weeks rather

7   than years.

8
9   The models of the autonomic visual reflexes and

10 interrelated aspects of visual perception

11 incorporated in the method and apparatus include the

12 property of the human optical system that perceives

13 stimuli of higher intensity earlier than stimuli of

14 lower intensity. This effect is primarily the

15 consequence of the integrating nature of the retina.

16 The longer a given brightness shines on a given area

17 of the retina the more photons are delivered to the

18 integration until eventually the threshold is

19 crossed, the speed of transit of visual stimuli

20 through the nerve and visual cortex to the brain is

21 also varied by the relative intensity.   This gives

22 rise to the phenomenon known as the "Pullfrich

23 effect" after the discoverer who described several

24 optical illusions for which the said intensity

25 dependent delay is responsible. It has been used as

26 a method for pseudo stereo image presentation. In

27 the prior art stimuli for visual field analysis have

28 been generally presented for a given fixed time as

29 well as a given brightness so that the threshold of

30 the retina could be determined. This required the

31 sequential and separate presentation of stimuli of

32 different brightness for any given point to

1   establish the threshold of the retina as in
2   US5024519 and others. Such a method is extremely
3   time consuming but hitherto the integration effect
4   precluded the possibility of simply delivering a
5   stimulus of increasing brightness at a given point
6   as there was no way to determine the precise moment
7   that the stimulus was perceived.
8
9   Conversely, in the present invention the eye's
10   saccade reflex is modeled in the computer timing so
11   that the moment of perception can be derived from
12   the time interval between the induced saccades. The
13   integration time is exploited to refine the accuracy
14   of the sensitivity measurement of the retina and
15   simultaneously minimize the duration of the test.
16   The equations below demonstrate how this is achieved
17   despite the fact that while the retinal integration
18   is exponential up to the retinal threshold the
19   Pullfrich delay continues to reduce linearly as the
20   stimulus becomes brighter. Hence the time from
21   presentation to the triggering of a saccade will be
22   tens of milliseconds longer for a dimmer stimulus
23   even if both stimuli integrate above the retinal
24   threshold in less than a millisecond. Conversely if
25   the stimuli took 200 ms or more to integrate above
26   threshold the latency delay before the saccade after
27   the retinal threshold is crossed would be much
28   longer than for the previous example so the
29   resulting total delay would be much longer
30   effectively amplifying the time difference between
31   saccades stimulated by different threshold levels of
32   different points on the retina.

1

2   In conventional static auto perimetry, stimuli are

3   presented for a fixed time and so deliver a fixed

4   energy to the retina. The patient is asked to press

5   a button or vocalise if they see a given stimulus at

6   a given point while fixating on a central fixation

7   point. Crucially they must suppress any reflex

8   saccade as best they can to any stimulus during the

9   test. This suppression is uncomfortable to achieve

10   and also causes a subconscious distraction that

11   reduces the patient's accuracy on an already

12   difficult task. Most auto perimeters offer two basic

13   types of test. In one type the stimuli are presented

14   at levels which are just below or just above the

15   expected threshold at a given point and the test is

16   repeated for each point in a "staircase" where if

17   the previous stimulus for a given point caused a

18   patient response then the next stimulus would be

19   presented at 2 to 3 times the desired amplitude

20   resolution below the previous stimulus, and so on

21   till the stimulus fails to generate a patient

22   response. Then a further stimulus is presented

23   halfway between the brightness of the last stimulus

24   that caused a response and the stimulus that failed

25   to cause a response. The final threshold value is

26   then set depending on whether or not the patient

27   responds to this stimulus. Obviously if the patent

28   had failed to respond to the first stimulus in the

29   sequence the next stimulus would be brighter rather

30   than dimmer and the overall sequence would be the

31   reverse of the above. Clearly this method takes a

32   long time, as each point in the retina will

1   typically need five stimuli to determine the
2   threshold. Most auto-perimeters offer an alternative
3   so called "supra threshold" test where each point in
4   the retina is presented at an amplitude calculated
5   on the basis of demographic ophthalmic data to be
6   just above the expected threshold for each point
7   thus a basic plot of areas below a chosen threshold
8   can be plotted. This method is relatively crude of
9   course and does not provide any detailed contour
10   data of the threshold sensitivity.
11
12   As will be obvious from the above, the stimuli are
13   inherently presented in the above tests at or close
14   to the patient threshold. Since the total energy of
15   the stimulus is critical this means that the stimuli
16   are either very dim or of very short duration. In
17   both cases the patient is required to respond
18   consciously to stimuli that in practice are
19   extremely ambiguous. The patient will constantly be
20   marginally aware of stimuli and be consistently
21   uncertain as to whether or not they "saw" a
22   stimulus. Patients report that this is extremely
23   stressful. Practice improves the patient's
24   confidence and so the reliability of the test but
25   such practice is not practical for a routine
26   diagnostic test. The test is further compromised
27   because it is inherently difficult to fixate on a
28   single point accurately. This has two consequences.
29   Clearly if the fixation point is uncertain, then the
30   positional accuracy of any test point on the retina
31   is equally uncertain; but the problem is made worse
32   by the fact that the eye's small movements around

1   the fixation mean that the total time a given

2   stimulus illuminates a given point on the retina is

3   variable and so the total integrated energy on that

4   point varies far more than is desirable. The above

5   issues are described to clarify the nature of the

6   present invention.

7

8   In the present invention the threshold of the retina

9   is determined by the delay between the presentation

10   of a stimulus and the triggering of a reflex saccade

11   to that stimulus. If the stimuli are of low

12   brightness then this time delay will include a

13   period of integration to the point where sufficient

14   energy has been delivered to the retina to pass the

15   threshold and a further delay caused by the

16   Pullfrich effect which makes a brighter stimulus

17   travel faster through the nerve path than a dimmer

18   stimulus. If the stimuli are of higher brightness

19   then the integration time will be shorter and the

20   Pullfrich delay will also be shorter because once

21   the retinal threshold is passed the energy is still

22   integrating on the retina and so the brighter

23   stimulus will travel through the nerve path very

24   much faster. This means that varying the brightness

25   of the stimuli will vary the average time of the

26   saccade response and so the resolution of the

27   amplitude measurement is determined by the

28   resolution of the measured time increment and the

29   chosen brightness. In principle it would be assumed

30   therefore that a dimmer stimuli set would provide a

31   more accurate measure of the retinal amplitude

32   sensitivity as a function of time. While this is

1   true to an extent, the present invention aims to

2   achieve a more accurate spatial plot as well as a

3   more accurate amplitude plot. It is central to this

4   invention that the accuracy of the eye fixation is

5   superior for a few hundred milliseconds post saccade

6   to its accuracy over a longer time therefore the

7   time resolution of the measurement must be balanced

8   against the deteriorating accuracy of the fixation

9   over time. Additionally if the test is delivered

10 close to the normal visual scanning saccade

11 frequency of between 1.2 and 5 saccades per second

12 the test will feel even more comfortable and natural

13 for the patient.

14

15 Thus in simplified terms, ignoring the integration

16 loss and limit and the precise function of the

17 Pullfrich delay which will be clarified later, the

18 time T between the commencement of a stimulus point

19 and the resulting saccade of the eye to that

20 stimulus is expressed by the function

21 Eq1:

22 $$T = \frac{(t^2 \cdot l + P)}{(t \cdot l)}$$

23 where t is the total time for the luminance "l" to

24 integrate to the detection threshold of the retina

25 and P is the Pullfrich delay for an arbitrarily

26 chosen luminance "h" where $h = t \cdot l$.

27

28 t can be derived from the function:

29 Eq2:

$$\left.\begin{matrix} \dfrac{-1}{(2\cdot l)}\cdot\left(-T\cdot l+\sqrt{T^2\cdot l^2-4\cdot l\cdot P}\right) \\[2ex] \dfrac{-1}{(2\cdot l)}\cdot\left(-T\cdot l-\sqrt{T^2\cdot l^2-4\cdot l\cdot P}\right) \end{matrix}\right] = t$$

Naturally the greater of the two solutions is the true result since clearly the arbitrarily chosen luminance is chosen to be greater than "l". Hence for any given level of light used as a stimulus the integration time t to h can be determined from the total time T. This means that relative sensitivity of the retina from one point to another is expressed directly as a function of t and can be derived from the interval time T and the resolution of the measure can be adjusted by increasing "l". The overall speed of the test and the average time between saccades can be adjusted for maximum comfort and accuracy by adjusting l to meet the criterion of average saccade time of between 200 and 800 ms described above.

The resulting value of t can be used directly to plot a relative sensitivity map of the retina. However, often it will be required to translate these relative values to commonly used units of measure of the retinal threshold sensitivity. In that case the functions of the retinal integration and the true function of the Pullfrich delay become important. A useful optional feature of the invention is that the stimulus can be increased or decreased in brightness from its initial presentation brightness, such an increase or decrease can be used to modify the function of T to

1 t to make the resulting function either more or less
2 linear as desired. Clearly in the absence of this
3 feature the dynamic range of the test would be
4 limited if the time intervals are limited as
5 required to maintain a natural rhythm. Increasing
6 the stimulus brightness during presentation is of
7 particular use in the testing of a subject with
8 known defects since the stimuli can be rapidly
9 increased in brightness once a predetermined
10 threshold is passed, thus speeding up the test on a
11 subject who would otherwise register a large number
12 of missed stimuli or take so long for each stimulus
13 that the natural comfort rhythm is broken.
14
15 The retinal integration function is quite complex as
16 discussed by T E Cohn of Berkeley in his paper
17 "Integration by the human eye; implications for
18 warning signal design". In the typical embodiment
19 of the invention the retinal integration to
20 threshold can be taken as above which follows the
21 standard Bloch's Law which states that the product
22 of intensity of a brief flash of light times the
23 time it is on is a constant at threshold. Beyond
24 Bloch's integrating time, usually taken as 0.1sec,
25 threshold declines only modestly as duration
26 increases until, for long durations, threshold is a
27 constant. This can be enhanced by a simple two-
28 limbed approximation to this threshold function
29 which obeys Bloch's law for short durations and
30 obeys the relation that threshold is constant for
31 longer durations. This is The Blondel-Rey law. It
32 is a simple way of summarising this two-limbed

1   function. It states that the product of a flash
2   intensity times its duration is equal to the
3   asymptotic threshold value times the sum of the
4   duration plus a visual response time constant
5   described above.
6
7   In certain embodiments of the invention where longer
8   time intervals are desired it may be considered
9   worthwhile to improve the accuracy of the system by
10   utilising the more accurate Blondel-Rey law, however
11   the error induced by the use of the less accurate
12   Bloch's Law at the ideal timing intervals
13   recommended for the method are in practice less than
14   errors due to the reflex variables in the eye and
15   so, while the overall error budget can be reduced by
16   the use of the most accurate integration formula,
17   the accuracy of the Bloch Law embodiment is still
18   substantially better than that achievable by the
19   staircase method in conventional auto perimetry.
20
21   The Pullfrich function is essentially linear
22   provided the stimuli are of sufficient brightness to
23   exceed threshold in less than 400 ms, so again the
24   best performance of the system will be achieved at
25   or close to the natural saccade rhythm of the eye in
26   scanning mode. This natural rhythm has been
27   determined by the inventors in a study of over 150
28   individuals to approximate, to within 20 ms, a value
29   defined as the subject's "natural counting rhythm".
30   It is well known that people tend to count much
31   faster than once per second and so various word
32   delays are recommended to lengthen the counting

1   rhythm to approximate a second more accurately when
2   people desire to time an event without a watch. The
3   inventors speculated that the natural rhythm would
4   inherently be proportional to the subject's
5   conscious reaction time. It proved to be that a
6   person's expressed maximum comfort zone in terms of
7   saccade frequency exactly matched the subject's
8   natural counting frequency to within 20 ms. This
9   proved to be true despite a variation of well over a
10 factor of two in different individuals' natural
11 counting rhythm and also to a similar variation for
12 a given individual in different states of fatigue or
13 arousal. This fact can be used by a practitioner
14 using the invention to set the ideal brightness of
15 the basic illumination level of the stimulus by
16 asking the patient to count up to ten or count aloud
17 the number of items on a screen presentation. The
18 faster the patient counts the brighter the basic
19 stimulus should be for maximum comfort in the test.
20 Alternatively the practitioner can use the count
21 test to determine the patient's level of anxiety and
22 arousal and may take steps to calm the patient until
23 they demonstrate a slower count rhythm and so allow
24 a slower and therefore higher resolution test.
25
26 It should be clear from the above that the accuracy
27 of the test can be enhanced by repeating the test
28 with different basic illumination levels, since the
29 threshold value for a given point and the
30 integration time should correlate exactly. In
31 general, however, it would not be necessary to
32 repeat the entire test; rather the test points for

1   any anomalous areas can be tested again at a
2   different brightness and the integration time
3   measured for that brightness can be correlated with
4   the original data. If the two values agree then the
5   value is certain: if they disagree a further test at
6   either of the two previous brightness levels or
7   alternatively at a third brightness level can be
8   applied. If this third test yields anomalous results
9   then the data should be discarded for that point but
10 in practice this occurs in less than one percent of
11 the test points.
12
13 A modified sequence of test stimuli can be presented
14 to create very high spatial resolution plots of a
15 defect perimeter. This is achieved by presenting a
16 sequence of stimuli in a line crossing the perimeter
17 defect alternating with randomly placed stimuli
18 elsewhere to prevent the patient recognising the
19 pattern. In a preferred embodiment at least some of
20 the alternate stimuli are placed to plot a line to
21 cross other suspected defect perimeter zones. In
22 this latter case there should be at least four plot
23 zones randomly sequenced or, if less than three
24 suspect zones exist, then one or more random stimuli
25 should be presented. It should be noted that such a
26 line of fractional degree difference plot points
27 would be impossible with a conventional central
28 fixation perimeter since the spatial pattern of the
29 plot points would be immediately apparent to the
30 patient. Conversely in the present invention each
31 stimulus that generated a saccade becomes the new
32 fixation point. Combined with the alternating random

1   or alternate zone stimuli this makes the overall

2   spatial pattern perceived by the subject entirely

3   random and unpredictable because, although the

4   stimuli are indeed occurring repeatedly on similar

5   points on the retina, the overall spatial position

6   of the stimuli as perceived by the subject is not

7   repeating.

8

9   In recent years an alternative to basic static

10   automated perimetry has been the frequency-doubling

11   test. One example of this method uses a stimulus

12   that consists of light and dark bars of a low

13   spatial frequency (0.25 cycle/degree), flickering in

14   counter phase at a high temporal frequency (25 Hz).

15   Briefly, the flickering produces an illusion of

16   doubling the spatial frequency of the stimulus. The

17   contrast of the stimulus is gradually increased and

18   the examined subject has to indicate when a movement

19   is perceived anywhere in the visual field. The

20   method is assumed to measure the integrity of a

21   particular subgroup of retinal ganglion cell,

22   sensitive to motion. This type of stimulus can be

23   used with the disclosed saccade trigger in a

24   sequence as described for the point stimulus above

25   where the stimulus changes to the fixation point

26   with each saccade. In this case again the absolute

27   threshold function for the contrast of the bars will

28   correlate to the time T as above and hence the range

29   of contrast needed for each presentation of the

30   frequency doubling stimulus target can be reduced,

31   because the stimulus need not initially be presented

32   below the contrast threshold since the time for the

1   saccade to the stimulus will indicate the relative

2   level above threshold of the contrast.

3

4   In a further embodiment of the invention the

5   relationship between the comfort frequency of the

6   scanning saccade and the normal human visual search

7   saccade frequency can be used to determine if an

8   individual has defects in the retina by presenting

9   each eye individually with pictures based on

10 principles laid out in detail below. These pictures

11 can be natural images or computer generated images

12 with selected regions of high and low spatial

13 frequency in addition to certain visual cues that

14 the inventors have defined which allow the priority

15 of a typical initial search saccade sequence to be

16 reliably predicted. Because in these special images

17 the initial gaze direction of the eye can be

18 predicted with a high reliability, and at least the

19 first saccade from that initial gaze fixation can

20 also be predicted, it means that in viewing these

21 images the presence of a high spatial frequency

22 feature on the image will cause the eye to be

23 attracted to it after the initial high priority cue

24 subsequent to the primary gaze fixation. In the

25 normal eye only the blind spot exists as an area

26 that obscures a feature that is revealed to the eye

27 when this initial saccade occurs. If an area of high

28 spatial frequency is revealed as the blind spot

29 moves this causes a change in both the saccade

30 priority AND causes the natural scanning rhythm to

31 "reset" to initial search mode. Since the initial

32 search saccade frequency is much more rapid than the

1   natural scanning frequency, any region of high
2   spatial frequency or other high priority cue
3   revealed as the eye initially saccades causing a
4   defect to cease to obscure the said cue will cause a
5   second burst of high frequency saccades as the eye
6   attempts to accommodate for its lack of expected
7   peripheral vision definition by scanning the
8   revealed cues with the fovea. This is an especially
9   useful test since it detects even quite shallow
10   anomalies in the eye even if the contrast
11   differential of the image is much higher than the
12   anomaly depth. The images are designed to cause
13   scanning saccades of relatively small amplitude but
14   the presence of an anomaly will cause a large
15   amplitude saccade as the fovea moves to accommodate
16   as described above, and hence both the frequency of
17   the saccades and the amplitude can be used to signal
18   the presence of an anomaly. In this case time from
19   the initial saccade to the triggered saccade is
20   inversely proportional to the depth of the saccade
21   because the differential between the anomaly and the
22   normal portion of the retina is equivalent in
23   practice to the contrast or differential above
24   threshold described for the previous tests in terms
25   of the relationship between stimulus and the speed
26   of the saccade reflex. The location of the saccade
27   spatial frequency cues can be set in a sequence of
28   images to digitally sequence the areas of interest
29   on the retina. For example eight images presented in
30   sequence can detect the presence of an anomaly one
31   64th of the visual field for each eighth of the
32   visual field tested in each image. Theoretically

1   this could be further refined by further subdivision
2   but in practice it is probably better to revert to
3   either frequency doubling or constant stimulus
4   plotting if detailed plotting is desired. This image
5   test is best used as an "instant" detector of the
6   presence or absence of anomalies worthy of more
7   detailed diagnosis.

8

9   Depending on the desire of the practitioner the
10 image colours can be chosen to cover either the full
11 spectrum or selected colours such as blue and yellow
12 that preferentially shows cone anomalies and is
13 therefore more sensitive to relatively small
14 pathologies of the eye.

15 The basic rules of the image design for predicted
16 priority sequence are as follows:

17 A solid perspective cue such as road, path or river
18 with a dark end point will draw the first gaze
19 fixation. This will be followed immediately by a
20 saccade to the darkest area of the image coupled
21 with any high spatial frequency data followed by a
22 saccade to the next highest spatial frequency region
23 that is also dark or to the highest spatial
24 frequency area of any brightness if there are no
25 more apparently dark areas of the image. These cues
26 should be set at least ten degrees apart. In a
27 normal vision subject these initial three saccades
28 will occur in less than 400 ms followed by much
29 slower "count" frequency saccades of less than 10
30 degrees amplitude as the eye assumes normal scanning

1   mode. If however any area of the eye has a defect

2   that uncovers an area of high spatial frequency then

3   the image effectively re-triggers the eye/brain

4   system to repeat the initial search sequence and so

5   the high frequency high amplitude saccades will

6   continue for at least twice the duration of a normal

7   vision subject.

8

9   Figs. 2 and 3 show representative figures as an

10 example to clarify the principles of the images.

11 Note that the real images may be computer generated

12 photo realistic images or abstract images. The

13 critical aspect is that they follow the principles

14 laid out here.

15

16 In Fig. 2, the first fixation is marked as 1 the

17 dark area at the end of the "perspective suggesting"

18 path. The area of the retina effectively under test

19 is 3 and the second fixation attractor is 2. In a

20 normal vision subject the spatial frequency

21 attractor at 3 does not change during the saccade

22 from 1 to 2 and so does not cause an immediate

23 saccade whereas if a defective area of the retina

24 obscured the high spatial frequency attractor at 3

25 when fixating on 1 then it would "appear" to the eye

26 immediately after the saccade to 2 and so trigger a

27 reflex saccade. It should be noted that should the

28 subject in fact saccade instead to 3 instead of 2

29 after 1, this obviously by definition demonstrates

30 that 3 was not under a region of low sensitivity or

31 resolution. This means that this type of test is

1   uniquely free from false positive results which is a

2   great advantage in any screening diagnostic test.

3   Fig. 3 illustrates the test being repeated for a

4   subsequent field.

5   A sequence of images covering the entire field

6   sector by sector can be presented to the patient.

7   The high spatial frequency sector should be no

8   greater than 0.25 degrees per cycle for the areas

9   outside the central ten degrees from the fovea.

10   Ideally the high spatial frequency sector should be

11   more than twice the average spatial frequency of the

12   rest of the image and regions less than half the

13   average spatial frequency should be avoided, as this

14   can tend to alter the saccade priority from the

15   ideal.

16   It should be noted that although the term

17   "perspective" is used this is not intended to mean

18   necessarily true perspective image. The human vision

19   system is so tuned to seek perspective cues that any

20   apparent taper however distorted will tend to be

21   read as a perspective cue. This has been shown in

22   our research to be almost always the primary cue in

23   an image since the brain seeks a sense of scale in

24   any image with an extremely high priority. However

25   areas that suggest shadows or doorways that may

26   obscure potential threats are very high priority

27   too. This proved to be so even with very young

28   subjects; the inventors suspect this is a

29   fundamental survival trait that is as genetically

30   programmed as the blink reflex is to an apparent

31   direct threat to the eye. The combination of a

1   "suggested perspective" cue and a dark "doorway" cue
2   is virtually 100 percent reliable as a trigger of
3   the first gaze fixation. In fact no subject in the
4   test trials ever failed to fixate first on such a
5   cue. Note that since the eye saccades to that first
6   cue from its previous rest position no feature of
7   the image is processed by the brain until after the
8   primary gaze fixation.

9   There are many other cues that the inventors have
10   researched that can be arranged in suitable priority
11   sequences to lend further variety to the test but
12   the above listed are adequate to create a successful
13   visual field defect diagnostic tool as disclosed
14   herein.

15   It should be obvious that instead of a sequence of
16   still images a moving image of many frames per
17   second could be used provided the said moving image
18   could be divided into two or three second sequences
19   where the saccade priorities of each such sequence
20   were known as above. In such a moving image method
21   stimuli that may cause the eye to enter pursuit mode
22   should be avoided.

23   In an alternative method a moving image sequence can
24   be used which is designed to exploit the pursuit
25   mode. In that case the pursuit stimulus should be
26   considered the primary fixation. Wherever the
27   pursuit stimulus comes to rest on the screen can be
28   defined for the still images above. In this case the
29   timing period used to discriminate considered as the
30   primary gaze fixation with the second and third
31   priority cues as normal from abnormal eye behavior

1   should be 2 to 3 second sequences free of the said

2   pursuit stimuli.

3   The apparatus may also be used to test for dyslexia

4   using the Fischer method of determining whether and

5   how well the patient is capable of reverse saccades

6   where the patient is instructed to saccade in a

7   direction OPPOSITE to the stimulus. In this

8   invention the method of the test is a presentation

9   of an image of for example the surface of a rabbit

10 warren. The patient is told that a dot will appear

11 just before a rabbit appears exactly opposite from a

12 moving fixation point and they must identify the

13 rabbit from a group of three recognisable "bunnies".

14 The fixation point is for example a bird or fox

15 image moving across the screen at any angle. A red

16 or other colour bright dot appears at some point and

17 within 50ms a rabbit appears for 100 to 150 ms

18 exactly opposite to the dot as measured through the

19 fixation stimulus. Normal subjects will in the

20 majority of cases register one saccade whereas

21 dyslexics will in general register two, one for an

22 aborted saccade to the initial stimulus they are

23 told NOT to look at and one for the correction to

24 the rabbit. This is because the ability of the

25 cognitive system to override the reflex to saccade

26 to any stimulus has proven to be consistent with the

27 absence of dyslexia whereas the inability to

28 override has proved to be an indication of the

29 opposite. In this invention the proposed

30 "recognition of the rabbit task" or similar

31 recognition task is a strong incentive to saccade as

32 early as possible to see the "rabbit" long enough to

1　recognise it. It is critical to the invention that

2　the features of the rabbit or other recognition task

3　that differentiate it from the other samples

4　previously shown with it to the subject must be of

5　such fine detail as to only be visible to the fovea.

6　If the person waits till the "rabbit" appears before

7　saccading then the saccade will arrive too late for

8　the brain to have time to image the rabbit

9　adequately for recognition. Hence simply suppressing

10　the reflex response to the red dot stimulus is not a

11　solution to the task.　Only if the subject saccades

12　opposite to the stimulus will the subject be looking

13　at the point where the rabbit appears and so get

14　enough time with the rabbit imaging on the fovea to

15　allow recognition. This requires that the eye is

16　capable of saccading at near reflex speed in the

17　opposite direction to the stimulus. This task is

18　possible at about 75 to 90 percent of the time for a

19　normal individual above the age of five. It is

20　impossible for children aged three or less and it is

21　virtually impossible for even mild dyslexics. For

22　example the set of rabbits in the test might be

23　drawn with one two or three sets of whiskers with an

24　apparent diameter of 0.1 to 0.3 degrees. In such a

25　case only the fovea would have sufficient resolution

26　to perceive the whiskers well enough to count them.

27

28　In a further embodiment of the invention, means are

29　provided to illuminate the eye preferably in the

30　infra red region capable of creating a clear

31　highlight on the cornea as viewed by a camera and

32　means whereby the camera delivers images in an

1   electronically interpretable way to a calculating
2   device such that the highlight reflections of the
3   cornea of both motion blurred and non blurred images
4   may be analyzed by commercially available software
5   algorithms to determine the angular moment of the
6   blur which in turn defines the direction of the
7   eye's movement causing the motion blur. Such means
8   are used to interpret the saccade results to confirm
9   that the saccades were induced by the stimulus and
10 not other distraction.
11
12 The test data can also be compared with a library of
13 data categorised for factors including age that
14 affect the normal sensitivity of the retina and a
15 second database of diseased and other abnormal
16 retinal data that may be compared to the measured
17 retinal data with a view to allowing a software
18 algorithm to suggest a possible diagnosis based on
19 said similarity by means of superposition of
20 perimeter and sensitivity data for each defect on
21 images of perimeters stored in the database of
22 diseased and other abnormal retinal data.
23
24 This can be done by assessing geometric
25 similarity to a set of images where the set
26 contains a majority of data from a given
27 disease or other abnormal category would
28 trigger the algorithm to suggest the majority
29 disease as the probable diagnosis, such
30 majorities being passed to a second database on
31 confirmation of the said diagnosis over time.
32 This second database is a refined rapid search

1 evolved version of the first database that may

2 be used preferably to the first when it exceeds

3 a sample size of at least 4 times the average

4 majority sample size.

5 Improvements and modifications may be incorporated

6 without departing from the scope of the invention as

7 defined in the claims appended hereto.